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| 10/723,955 | 11/26/2003 | Ruoping Chen | AREN-007CON2(7.US29.CON) | 3273 |

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| EXAMINER | |
|---|---|
| LI, RUIXIANG | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

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| 10/13/2010 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/723,955 | CHEN ET AL. | |
| | Examiner | Art Unit | |
| | RUIXIANG LI | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *69-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/10/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### Status of Application, Amendments, and/or Claims

Applicant's amendment filed on 09/10/2010 has been entered. New claim 88 is added. Claims 69-88 are pending and under consideration.

### Information Disclosure Statement

The information disclosure statement filed on 09/10/2010 has been considered by the Examiner and a signed copy of the form PTO-1449 is attached to the office action.

### Claim Rejections under 35 USC § 101 and 112, 1st paragraph

(i). 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

(ii). Claims 69-87 are rejected under 35 U.S.C. 101 and 112, first paragraph because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. New claim 88 is also rejected on the same basis. The basis for the rejection is set forth in the previous office action.

Claims 69-88 are drawn to a method of screening for a compound that increases cAMP levels in peripheral blood leukocytes. The claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. A specific and

substantial utility is one that is particular to the subject matter claimed and that identifies a "real world" context of use for the claimed invention which does not require further research.

First, since the claims are directed to a specific method of use, the utility of the claims are limited to that use. Consequently, there is no "well-established" utility for the method (See REVISED INTERIM UTILITY GUIDELINES TRAINING MATERIALS, Example 12, on page 63. http://www.uspto.gov/web/patents/guides.htm)

Secondly, there is no specific and substantial utility for the orphan human TDAG8 receptor of SEQ ID NO: 82, the compound to be identified by the method, and thus a method of screening for a compound. The human TDAG8 receptor of SEQ ID NO: 82 is an orphan receptor and has no known ligand and is not linked to any known biological functions, any known diseases or medical conditions. It clearly requires further research for an artisan to confirm a "real world" context of use, that is, to determine the biological functions of the orphan human TDAG8 receptor used in the screening method of the present invention and a use for the compound to be identified by the claimed screening method in a patent sense.

Furthermore, MPEP§2107.01 clearly lists that a method of assaying for or identifying a material that itself has no specific and/or substantial utility does not have a specific and substantial utility.

Accordingly, the rejections of claims 69-88 under 35 U.S.C. 101 & 112, 1st paragraph due to lack of a patentable utility are maintained.

(iii). Response to Applicants' argument

Applicants argue that in view of the fact that: a) TDAG8 is preferentially expressed in organs containing immune cells; b) activation of TDAG8 by agonists, such as ATP and ADP, leads to an increase in intracellular cAMP accumulation; c) elevated cAMP accumulation in peripheral blood leukocytes inhibits inflammation; and d) the role of ATP in mediating inflammation is known, it follows that the utility of TDAG8 would be readily apparent to one of skill in the art.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. Applicants' argument is based upon the following assumptions: TDAG8 is expressed in peripheral blood leukocytes, ATP or ADP binds and activates TDAG8, leading to an increase in intracellular cAMP accumulation, which inhibits inflammation in peripheral blood leukocytes. However, there is no evidence showing that TDAG8 mediates inflammation in peripheral blood leukocytes. In a poster presentation by some of the inventors of the instant application dated on 2000 (see IDS submitted on 08/30/2005), Applicants suggests that ATP binds TDAG8 and causes apoptosis of thymocytes. Now, Applicants argue that ATP binds TDAG8 and mediating inflammation in peripheral blood leukocytes, clearly indicating that Applicants have no idea of what the functional activity of TDAG8 has and that Applicants are purely guessing about the functional role of TDAG8.

Applicants argue that TDAG8 is preferentially expressed in organs containing immune cells. This is not really true. Thymus, a primary lymphoid organ, comprises T cells, B cells, but the cDNA of TDAG8 in thymus was not detected under the conditions; on the other hand, there was a much stronger band at 450bp in the liver (Figure 6). Moreover, the specification does not provide any evidence showing the TDAG8 protein was actually expressed in the tissues in a manner corresponding to the detection results in Figured 6.

Applicants argue that activation of TDAG8 by agonists, such as ATP and ADP, leads to an increase in intracellular cAMP accumulation. However, such an assay was done in 293 cells, not in peripheral blood leukocytes. Activation of any Gs-coupled GPCR results in an increased cAMP accumulation, regardless what the initial stimulation is. It is also noted that Applicants' argument that increased constitutive activity of TDAG8 leads to an increase in cAMP accumulation is incorrect. Figures 5A and 5B show that increased constitutive activity of TDAG8 leads to an increase in intracellular IP3 accumulation.

Applicants argue that elevated cAMP accumulation in peripheral blood leukocytes inhibits inflammation, referring to publications including Moore et al. (Clin. Exp. Immunol. 101:387-389, 1995). This is not persuasive because Moore et al. teach that cAMP acts as an intracellular second messenger for a variety of hormones, inflammatory mediators, and cytokines. Moore et al. also teach that production of cAMP

in leukocytes is stimulated by β-adrenergic catecholamines, histamine and the E series prostaglandins by a receptor-coupled activation of adenylate cyclase (page 387, left column, the 2nd paragraph). Thus, the particular function of cAMP in leukocytes taught by Moore et al. does not render the TDAG8 a particular biological function.

Applicants argue that the role of ATP in mediating inflammation is known, referring to publications, including Brake et al. (Chemistry and Biology 3:229-232, 1996). This is not persuasive because Brake et al. teach that ATP modulates a plethora of physiological states and cellular responses, including vascular ton, electrolyte transport, mast cell degranulation, and synaptic transmission in the central nervous system and periphery. ATP exerts its actions by binding to a family of functionally distinct cell-surface receptors (page 229, left column, the first paragraph). Thus, the role of ATP in a particular cell depends upon the particular receptor; ATP has different roles in a particular cell when it binds to different receptors. In this regard, Gloriam et al. teach that many members of Rhodopsin family, which have diversified functions, can be activated by ATP and ADP (Gloriam et al, Biochimica et Biophysica Acta., 1722: 235-246, 2005; in particular 235, left column). Therefore, the biological effect of cAMP depends on not only the initial stimulation, but also the cell type and the particular receptor. Thus, the biological functions of ATP, ADP or cAMP known in the art do not automatically render the instant TDAG8 a particular role in mediating inflammation in peripheral blood leukocytes.

Clearly, the specification fails to show that TDAG8 mediates inflammation in peripheral blood leukocytes. It requires further research for an artisan to confirm a "real world" context of use, that is, to determine the biological functions of the orphan human TDGA8 receptor of SEQ ID NO: 82 and thus a specific and substantial utility for the compound to be identified by the instantly claimed method.

Accordingly, claims 69-88 are rejected under 35 U.S.C. 101 & 112, 1st paragraph due to lack of a patentable utility.

**Conclusion**

No claims are allowed.

**Advisory Information**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.
October 2, 2010